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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/134,771	08/12/1998	DINAH W.Y. SAH	860098.425	8421

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EXAMINER	
KAUSHAL, SUMESH	23
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/134,771	Applicant(s) SAH ET AL.	
	Examiner Sumesh Kaushal	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *16-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/25/02 has been entered.

Claims 1-26 were pending. Claims 16-22 were withdrawn from further consideration as being drawn to a non-elected invention. Claim 1 was amended. Claims 25-26 were newly filed. Claims 1-15 and 23-26 were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Some references cited herein are of record in a prior Office action.

Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection below as necessitated by the recent amendments.

Claim Objections

Claims 25 and 26 are objected to because of the following informalities: The instant claims recite limitation "agent" whereas the claims list more than one agent (not in alternative). Appropriate correction is required.

Claim Rejections - 35 USC 103

Claims 1-15 and 23-26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Hosimaru et al (PNAS. 93:1518-1523, 1996) and Prasad et al (In Vitro. Cell Dev. 30A:596-603, 1994) in view of Boss et al (US 5411883, 1995) and Gallyas et al (Neurochem. Res. 22(5):569-575, 1997) and further in view of Casper et al (J Neurosci. Res. 30(2):372-81, 1991) and Nikkhah et al (Exp. Brain Res. 92(3):516-23, 1993).

The applicant argues that there is no suggestion or motivation to combine the cited references and there is no reasonable expectation of success. The applicant argues that a person skill in the art would not expect that the method of immortalizing rat neuronal progenitor as taught by Hosimaru et al would also work for human mesencephalonic neuronal cell progenitors Furthermore, Hosimaru et al teaches the use of FGF where as the present invention uses EGF or PDF. The applicant further argues that Prasad et al does not suggest that BSA, albumin, fibronectin and collagen would be necessary for the proliferation of mesencephalon progenitor cells. The applicant further argues that Boss et al does not teach progenitor cells that grow in to a monolayer culture. The applicant further argues that characterization of GABA-ergic and dopamine neurotransmitters as taught by Gallyas et al is not related to invention as claimed. The applicant concluded that combination of the cited references does not teach or suggest the immortalization of human mesencephalon neuronal progenitor cell lines that are capable of differentiation into GABaergic and dopaminergic cells.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The applicant has failed to consider the combined teaching of the reference cited herein in entirety. The combination and modification of the teachings of the prior art clearly suggested the claimed invention.

In this case, Hosimaru et al teaches immortalized rat neuronal progenitor cells wherein the expression of v-myc oncogene is driven by a tetracycline-controlled trnsactivator and a human cytomegalovirus (CMV) promoter. The cited art teaches that the cells were first cultured in a serum supplemented media follow by culturing in serum free media containing growth factors. Hosimaru et al teaches the culturing and selection of the cells onto polyornithine/laminin-coated tissue culture plates. In addition, Hosimaru et al further teaches that presence of several cytokine, or forskolin or growth factors on a specific substrate is required for the differentiation of immortalized neuronal precursor cells (page 1518, abstract; page 1519, col.1. para.3; page 1522, col.1, para.2). Prasad et al teaches the isolation of an immortalized dopamine-producing nerve cell line derived from fetal rat mesencephalic tissue transfected with an oncogene (see abstract). Hosimaru et al and Prasad et al does not teach the immortalization of a human neuronal precursor cell, wherein the cell is capable of differentiating into a dopaminergic and/or GABA-ergic neurons.

Casper et al teaches that Epidermal growth factor (EGF) enhances the survival of dopamine neurons in rat embryonic mesencephalon primary cell culture. Similarly, Nikkhah teaches that Platelet-derived growth factor (PDGF) promotes survival of rat and human mesencephalonic dopaminergic neurons in culture.

Boss et al teaches the isolation and culture methods for the proliferation of human mesencephalon neuron progenitor cells, wherein the cultured neuronal cells differentiate to produce dopamine-producing cells (see abstract; col.6, line 33; col.9-10, table 1-3; col.20 line 60). In addition, Boss et al clearly teaches the isolation and monolayer culture of human mesencephalon neuron progenitor cells (see abstract; preparation of monolayer culture, col.20 line 60).

Gallyas et al teaches the characterization of mouse immortalized neuronal cell lines by measuring the concentration of various neurotransmitters, like GABAergic and dopamine (see abstract; page 570, col.2, para 3; page 571, table-I, fig-1; page 572, table-II).

Thus, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immortalized rat neuronal progenitor cells as taught by Hosimaru et al and Prasad et al with human mesencephalon neuron progenitors cells as taught by Boss et al. It would have been further obvious to characterize immortalized human mesencephalon cells as taught by Gallyas et al because dopamine and GABA are neurotransmitter of interest. It would have been further obvious to use EGF and PDFG to promote the survival of mesencephalonic dopaminergic neurons in culture as taught by Casper and Nikkhah. One would have been motivated to make immortalized human neuronal progenitor cells wherein the expression of v-myc oncogene is driven by tetracycline-controlled trnsactivator because the suppression of v-myc oncogene in an immortalized progenitor induces the differentiation of the neuronal progenitor cell. One would have been also motivated to make immortalized human neuronal progenitor cells because the human neuronal cells would have been useful in the study of neurotransmitters and neuron cell differentiation. In addition, one would have a reasonable expectation of success because mesencephalon cells are easy to transfect, especially in the presence of growth factors like EGF and PDGF which promotes mesencephalon cell survival. Furthermore, in view of cited art phenotypic characterization of neuronal cells has been considered routine in the art at the time of filing. Thus, the invention as claimed is prima facie obvious in view of prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-

6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Tracey Johnson, whose telephone number is (703) 308-0377.

If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 *(http://www.uspto.gov)* and **A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED** to facilitate further examination.

SUMESH KAUSHAL
Patent examiner

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER